

REMARKS

Reconsideration and withdrawal of the rejections of the application are respectfully requested in view of the remarks and amendments herein.

I. STATUS OF THE CLAIMS AND FORMAL MATTERS

Claims 1-14 and 18-53 are now pending, and claims 14, 18-26, and 52-53 are under examination. Claims 14 and 18-23 have been amended, claims 15-17 have been cancelled, and new claims 52-53 have been added, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents.

No new matter is added.

It is submitted that these claims are and were in full compliance with the requirements of 35 U.S.C §112. In addition, the amendment and remarks herein are not made for the purpose of patentability within the meaning of 35 U.S.C. §§101, 102, 103 or 112; but rather the amendments and remarks herein are made simply for clarification and to round out the scope of protection to which Applicants are entitled. Specifically, support for the amendments can be found throughout the specification, including page 17, lines 1 to 3 as originally filed, and in the claims as originally presented.

II. THE REJECTIONS UNDER 35 U.S.C. §112 ARE OVERCOME

Claims 20, 22 and 23 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite.

Specifically, claims 20 was rejected as lacking antecedent basis for the recitation “the atheroprotective lipid profile”, and claims 22 and 23 were rejected as lacking antecedent basis for the recitation “reduces 11 β -HSD1 activity”. Further, claim 23 was rejected as containing a misspelling.

Applicants respectfully assert that the amendments herein have amended claims 20, 22 and 23 to ensure that antecedent basis exists for all recitations, and to remove spelling errors. Accordingly, the rejections are now moot.

Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. §112, second paragraph, is respectfully requested.

III. THE ART REJECTIONS ARE OVERCOME

Claims 14-25 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Gordon et al. as evidenced by Apostolova et al. Claim 26 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Gordon et al., and further in view of Hermanowski-Vosatka et al. The rejections are respectfully traversed.

Applicants respectfully remind the Examiner that a two-prong inquiry must be satisfied in order for a Section 102 rejection to stand. First, the prior art reference must contain all of the elements of the claimed invention, *see Lewmar Marine Inc. v. Barient Inc.*, 3 U.S.P.Q.2d 1766 (Fed. Cir. 1987), and, the single prior art reference must contain an enabling disclosure, *see Chester v. Miller*, 15 U.S.P.Q.2d 1333, 1336 (Fed. Cir. 1990).

It is respectfully submitted that the cited reference fails to disclose each and every element of the pending claims.

Regarding the obviousness rejection, Applicants respectfully remind the Examiner that establishing a *prima facie* case of obviousness requires three basic criteria: there must be some suggestion or motivation in the cited art to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art references must teach or suggest all the claim limitations. MPEP 2143.

The Examiner is also respectfully reminded of the case law, namely, that there must be some prior art teaching which would have provided the necessary incentive or motivation for modifying the reference teachings. *In re Laskowski*, 12 U.S.P.Q. 2d 1397, 1399 (Fed. Cir. 1989); *In re Obukowitz*, 27 U.S.P.Q. 2d 1063 (BOPAI 1993). Further still, "obvious to try" is not the standard under 35 U.S.C. §103. *In re Fine*, 5 U.S.P.Q. 2d 1596, 1599 (Fed. Cir. 1988). And, as stated by the Court in *In re Fritch*, 23 U.S.P.Q. 2d 1780, 1783-1784 (Fed. Cir. 1992): "The mere fact that the prior art may be modified in the manner suggested by the Office Action does not make the modification obvious unless the prior art suggests the desirability of the modification."

Also, the Examiner is respectfully reminded that for the Section 103 rejection to be proper, both the suggestion of the claimed invention and the expectation of success must be founded in the prior art, and not Applicants' disclosure. *In re Dow*, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988). Furthermore, it has recently been reaffirmed by the Supreme Court in KSR that the factors set out in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18: "[T]he scope and content of the prior art are determined; differences between the prior art and the claims at

issue are...ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented.” *KSR International Co. v. Teleflex Inc.*, 550 U.S. ____ (2007).

The obviousness rejection combines Gordon et al. with Hermanowski-Vosatka et al. Applicants respectfully submit that none of these references, either alone or in any combination thereof teach or suggest the claimed invention.

The present claims relate to a method for reducing cardiovascular disease risk in an animal at risk of cardiovascular disease, comprising administering to said animal a pharmaceutically effective amount of an agent which directly inhibits 11 β -HSD1 protein synthesis or activity. That is, the present claims relate to a method that requires that the agent inhibits 11 β -HSD1 at the protein level, i.e. either by inhibiting production of the protein from mRNA or by directly inhibiting the enzyme itself. Applicants respectfully submit that none of the cited references teach or suggest such a method.

As stated above, the Office Action rejected claims 14 to 25 over Gordon *et al* as evidence by Apostolova *et al*. Gordon states that DHEA (dehydroepiandrosterone) reduces atherosclerosis. However, Gordon is silent on the mechanism by which DHEA achieves this effect. In particular, Gordon provides no suggestion that 11 β -HSD1 is involved in the reduction of atherosclerosis following DHEA administration.

The Office Action relies on the post-published Apostolova citation as disclosing that DHEA reduces 11 β -HSD1 activity. The Office Action specifically refers to the published abstract of Apostolova, which states that “DHEA causes downregulation of 11 β -HSD1 and dose-dependant reduction of its oxoreductase activity”. Applicants respectfully submit that the reference, if it is to be relied upon, must be considered as a whole. Attached is a copy of the full Apostolova reference.

The Examiner’s attention is respectfully drawn to Apostolova at page E 959, left hand column, wherein it is stated that DHEA induces down regulation of 11 β -HSD1 mRNA expression. The right hand column on page E 959 further states that DHEA also reduced 11 β -HSD1 oxoreductase activity. However, Apostolova teaches in the last seven lines of the

paragraph entitled “DHEA-induced inhibition of 11 β -HSD1-dependant oxoreduction of 11 β -dehydrocpiandrosterone in 3T3-L1 adipocytes” that:

“Furthermore, DHEA did not exert a direct inhibitory effect on 11 β -HSD1 activity,... Together, these results indicate that DHEA decreases 11 β -HSD1 activity by inhibition of gene expression”.

That is, Apostolova clearly teaches that DHEA does not act as an inhibitor at the protein level, but rather by inhibition of gene expression.

This is in direct contrast to the presently claimed method, which requires that agent inhibits 11 β -HSD1 protein synthesis or activity, i.e. that the inhibitor works at a protein level, not by decreasing mRNA expression.

Thus, Gordon et al. as evidenced by Apostolova et al. fails to teach each and every element of the pending claims, such that the rejection cannot stand. Reconsideration and withdrawal of the Section 102 rejection is therefore respectfully requested.

Turning to the obviousness rejection of claim 26, Applicants respectfully submit that there is no teaching or suggestion in the cited references to use an inhibitor of 11 β -HSD1 which works at the protein level in order to reduce cardiovascular disease risk. Since the Gordon reference does not disclose the mechanism of action of DHEA, and says nothing about its effect on 11 β -HSD1, it would not lead a skilled person to a method that requires the agent to inhibit 11 β -HSD1 protein expression or activity. Any alleged inherent effect of DHEA on 11 β -HSD1 via regulation of gene expression is not revealed by Gordon, and thus could not suggest to a skilled person to alternatively inhibit the enzyme at the protein level. Further, as indicated above, the Apostolova reference, while not qualifying as a reference under §102 or §103 fails to remedy the deficiency of Gordon et al. Similarly, nothing in Hermanowski-Vosatka remedies the deficiencies of Gordon et al. There is no motivation, suggestion, or teaching in any of the references to lead the skilled artisan to the claimed method, which requires that agent inhibits 11 β -HSD1 protein synthesis or activity, i.e. that the inhibitor works at a protein level, not by decreasing mRNA expression.

As none of the cited references provide any suggestion, motivation, or teaching that would direct one of skill in the art to the claimed method, and as any such combination of the references would not arrive at the claimed method, the rejection under Section 103 cannot stand.

Reconsideration and withdrawal of the rejection under 35 U.S.C. §103 is therefore respectfully requested.

REQUEST FOR INTERVIEW

If any issue remains an impediment to allowance, a further interview with the Examiner is respectfully requested and the Examiner is additionally requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

CONCLUSION

Favorable reconsideration of the application as amended herein and prompt issuance of a Notice of Allowance, or an interview at a very early date with a view to placing the application in condition for allowance, are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date.

Respectfully submitted,

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